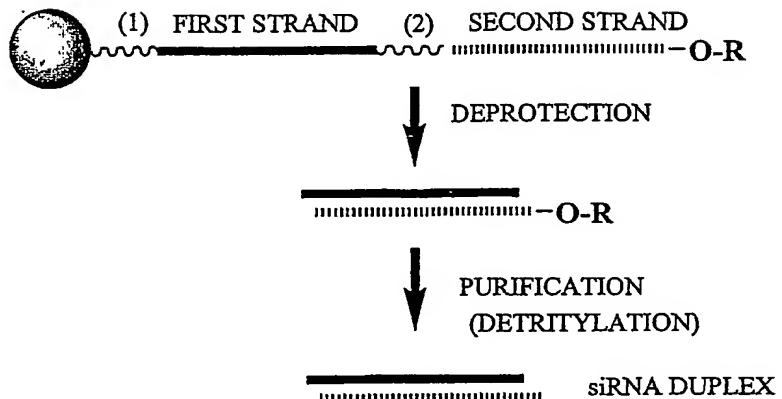


Figure 1

= SOLID SUPPORT

R = TERMINAL PROTECTING GROUP
FOR EXAMPLE:
DIMETHOXYTRITYL (DMT)

(1) = CLEAVABLE LINKER
(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR
INVERTED DEOXYABASIC SUCCINATE)
(2) = CLEAVABLE LINKER
(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR
INVERTED DEOXYABASIC SUCCINATE)

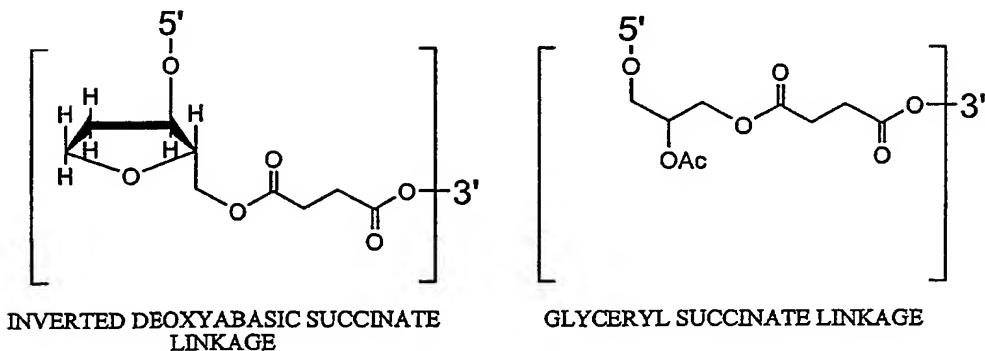


Figure 2

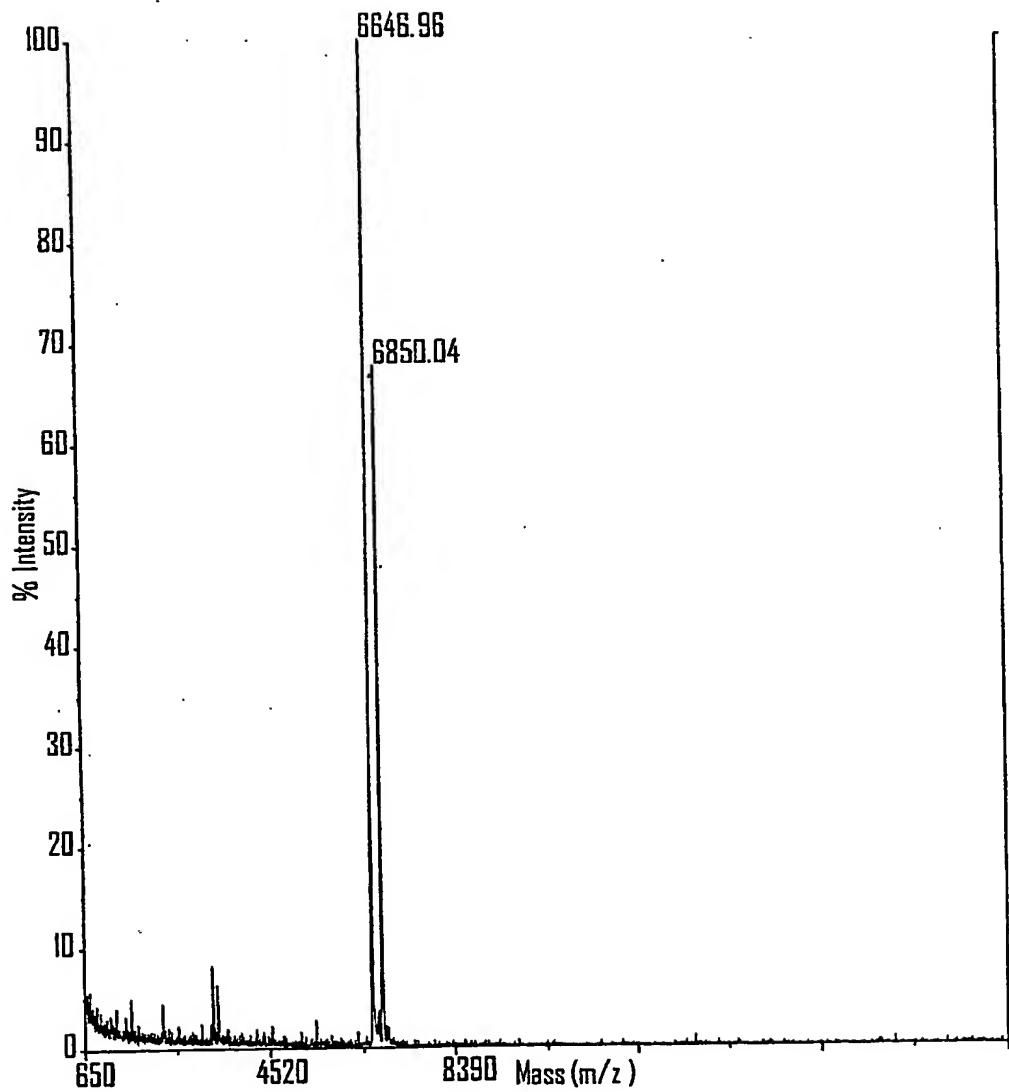


Figure 3

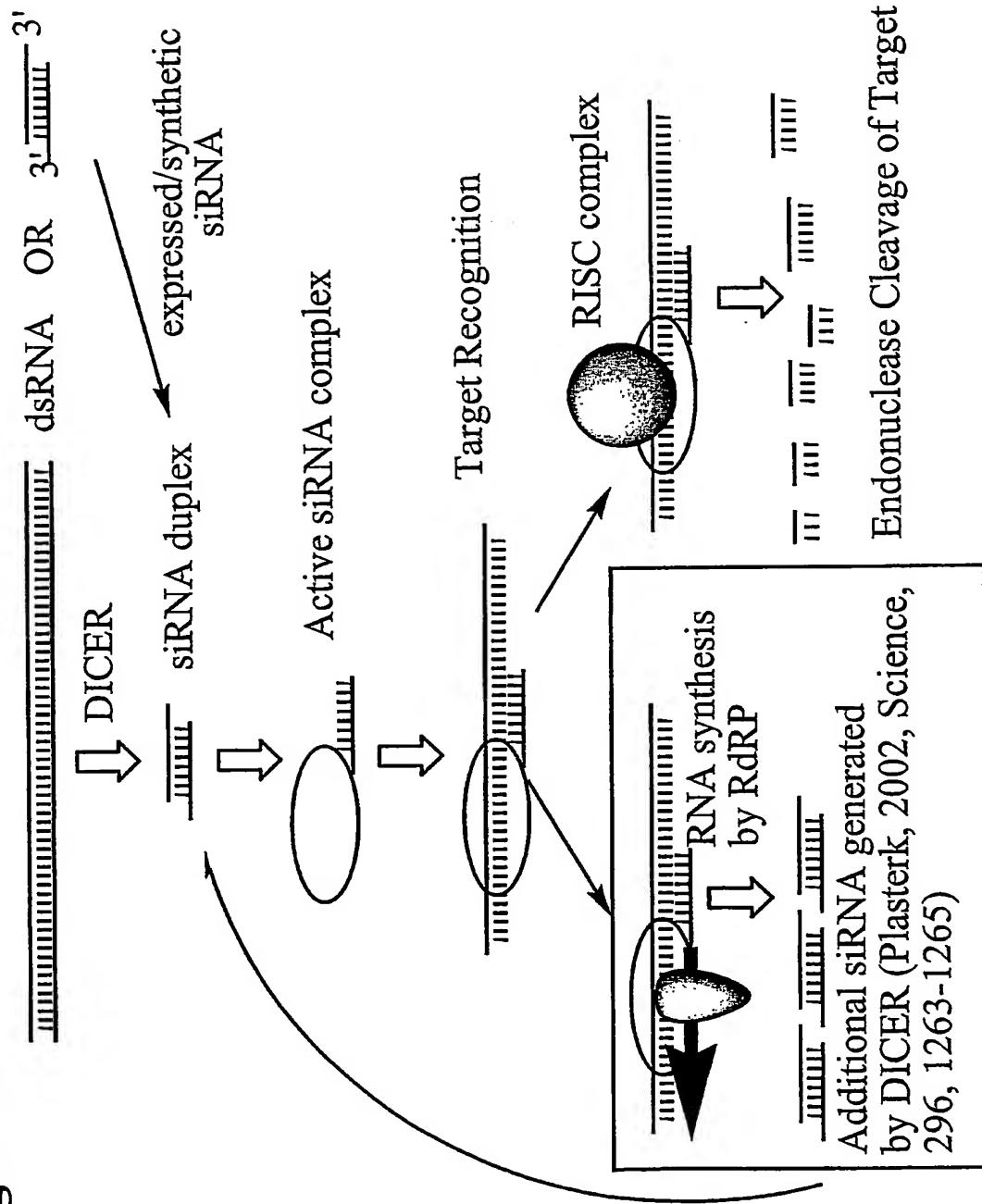
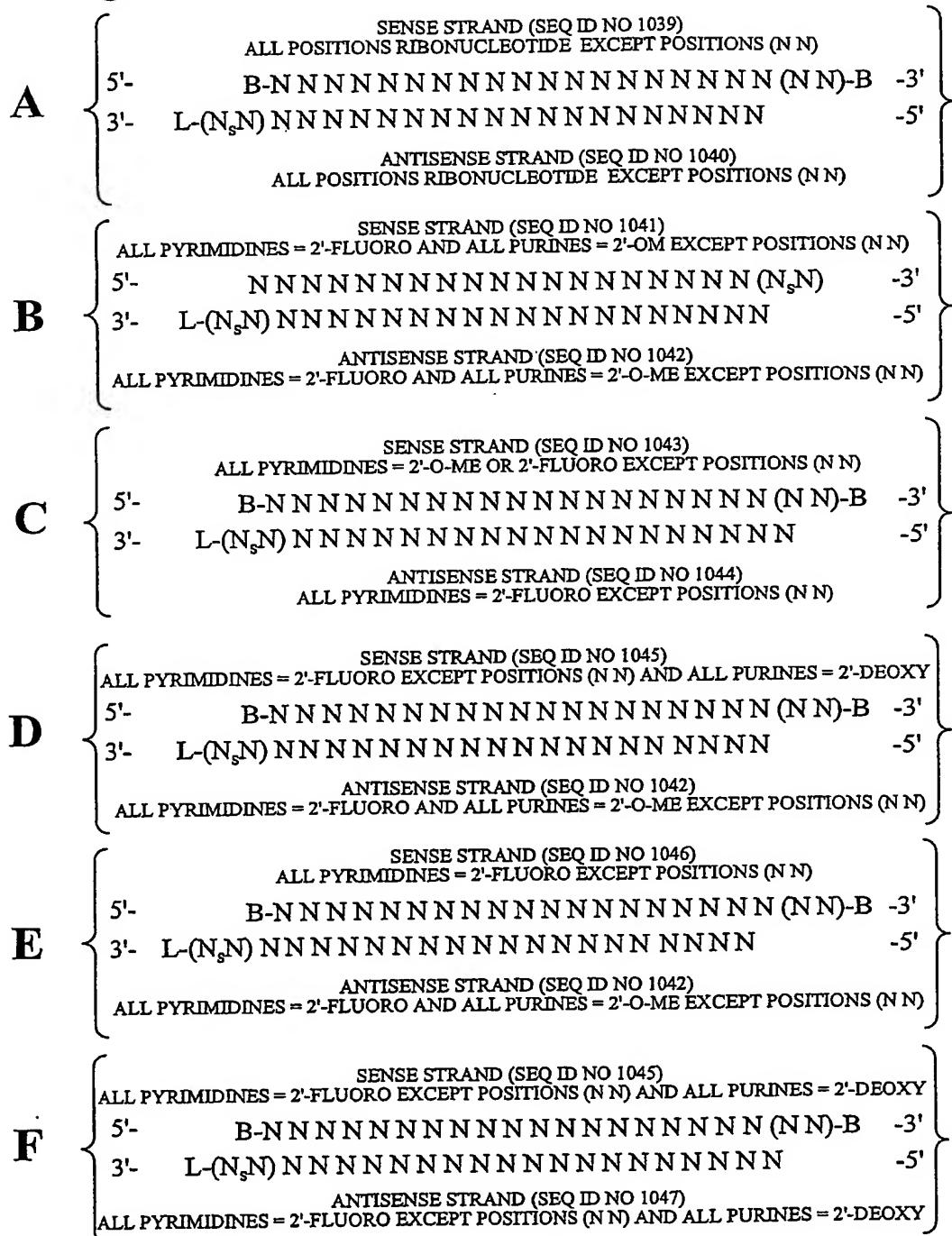


Figure 4

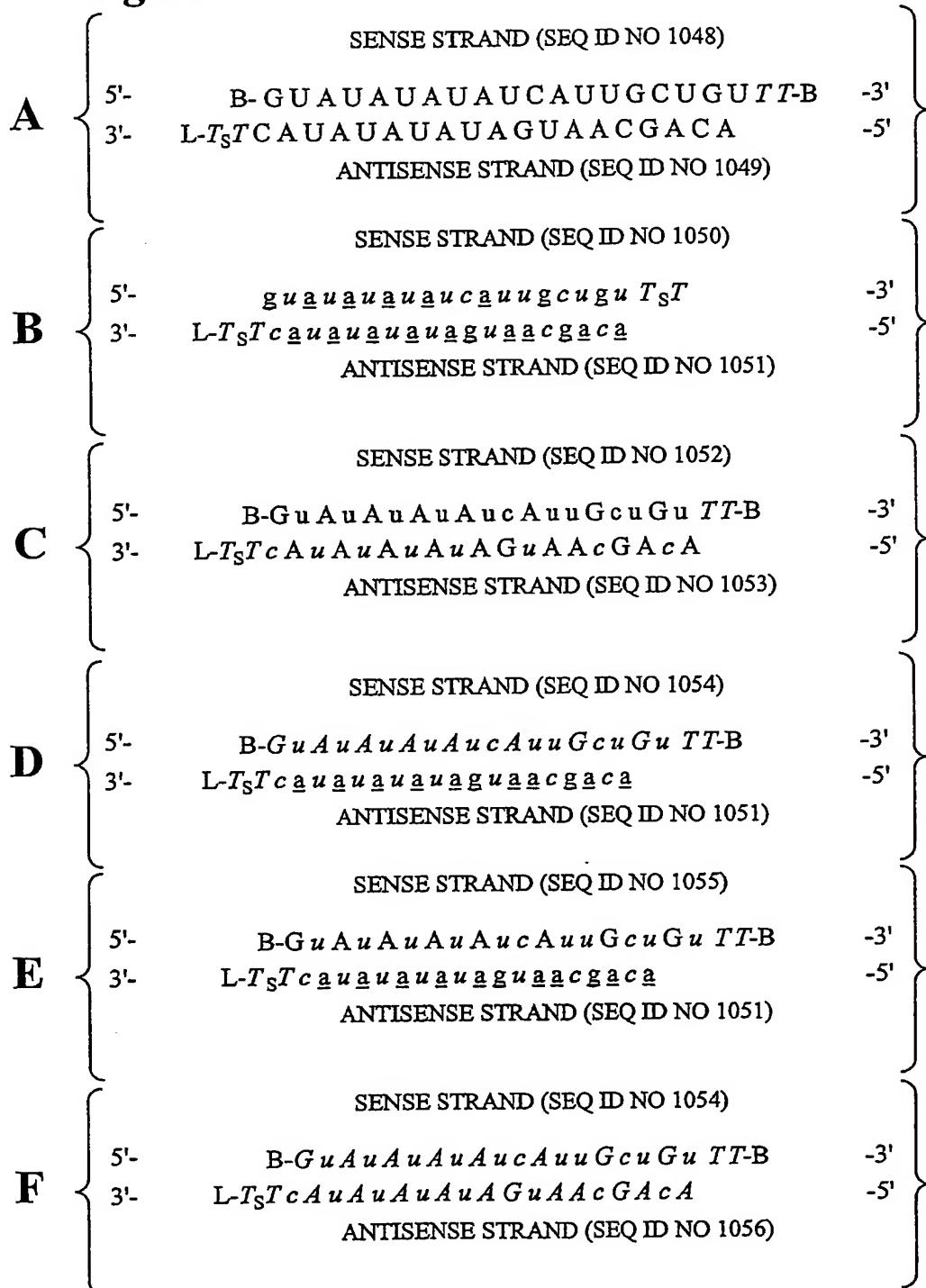


POSITIONS (NN) CAN COMprise ANY NUCLEOTIDE, SUCH AS DEOXYNUCLEOTIDES (e.g. THYMIDINE) OR UNIVERSAL BASES

(e.g. THYMIDINE) OR UNIVERSAL BASES
B = ABASIC, INVERTED ABASIC, INVERTED NUCLEOTIDE OR OTHER TERMINAL CAP
THAT IS OPTIONALLY PRESENT.

L = GLYCERYL MOIETY THAT IS OPTIONALY PRESENT

L = GLYCERYL MOIETY THAT IS OPTIONALLY PRESENT
 S = PHOSPHOROTHIOATE OR PHOSPHORODITHIOATE THAT IS OPTIONALLY ABSENT

Figure 5

lower case = 2'-O-Methyl or 2'-deoxy-2'-fluoro

italic lower case = 2'-deoxy-2'-fluoro

underline = 2'-O-methyl*ITALIC UPPER CASE = DEOXY*B = ABASIC, INVERTED ABASIC, INVERTED
NUCLEOTIDE OR OTHER TERMINAL CAP THAT
IS OPTIONALLY PRESENT

L = GLYCERYL MOIETY OPTIONALY PRESENT

S = PHOSPHOROTHIOATE OR
PHOSPHORODITHIOATE THAT IS OPTIONALY
ABSENT

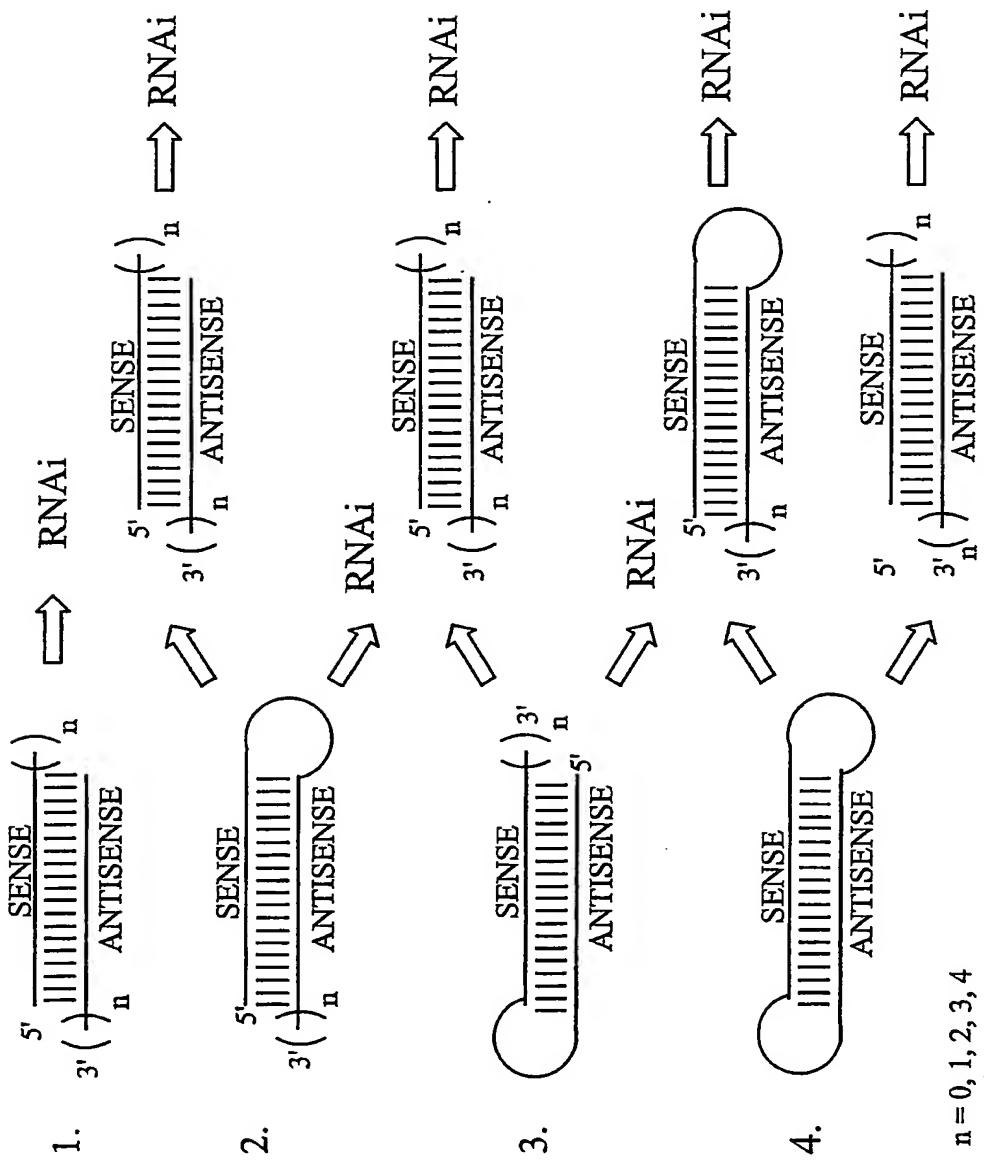
Figure 6

Figure 7

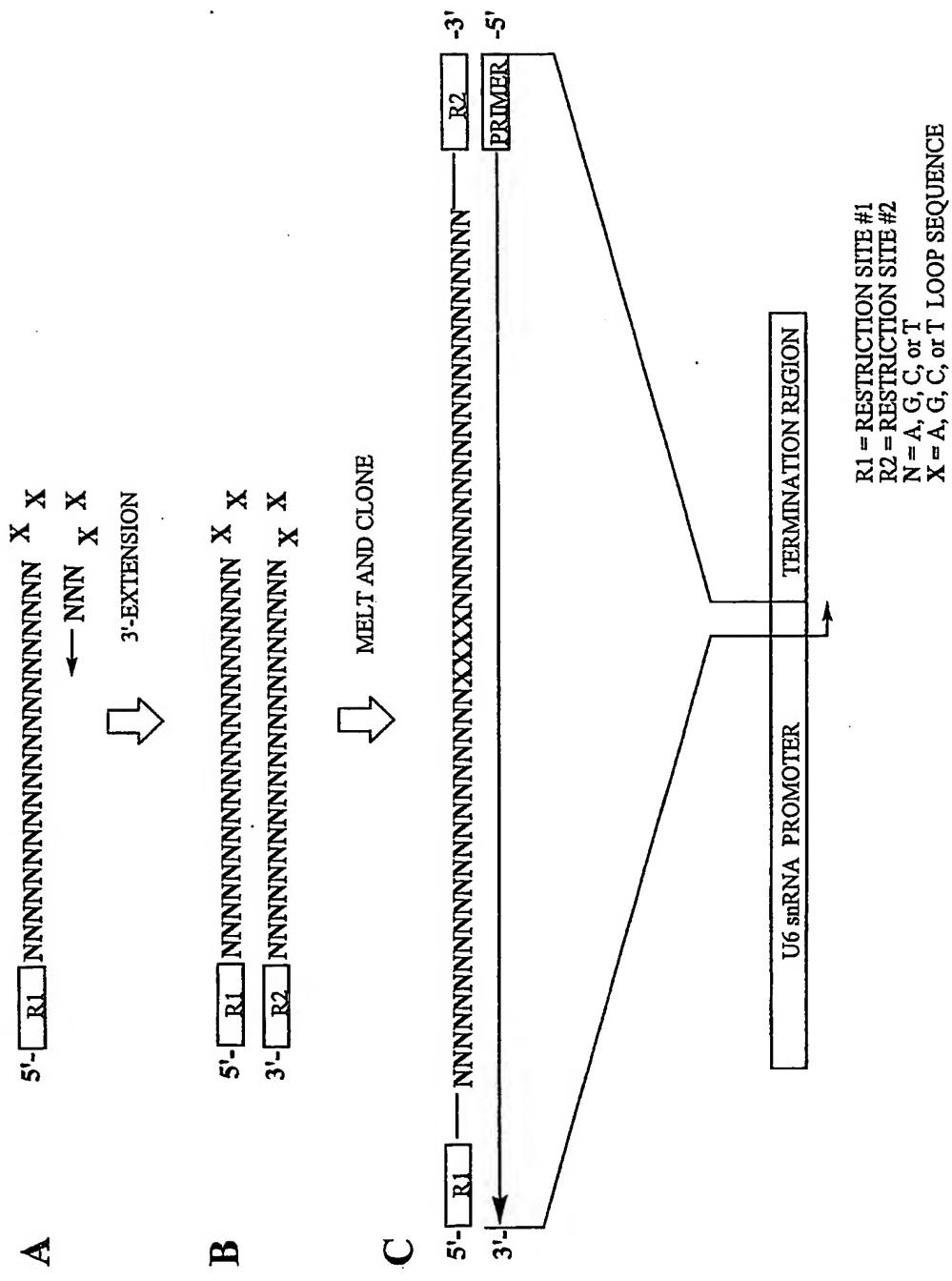


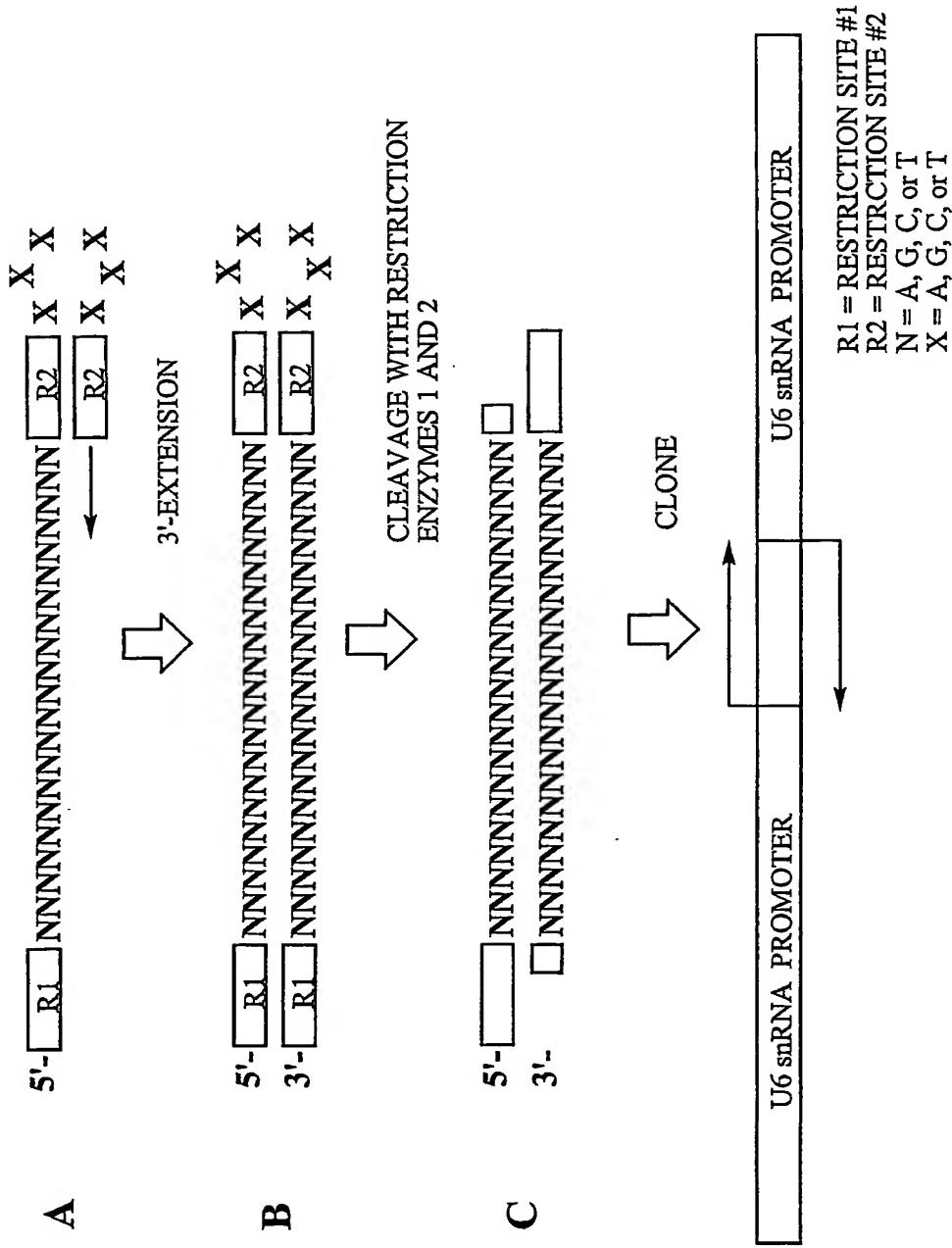
Figure 8

Figure 9: Target site Selection using siRNA

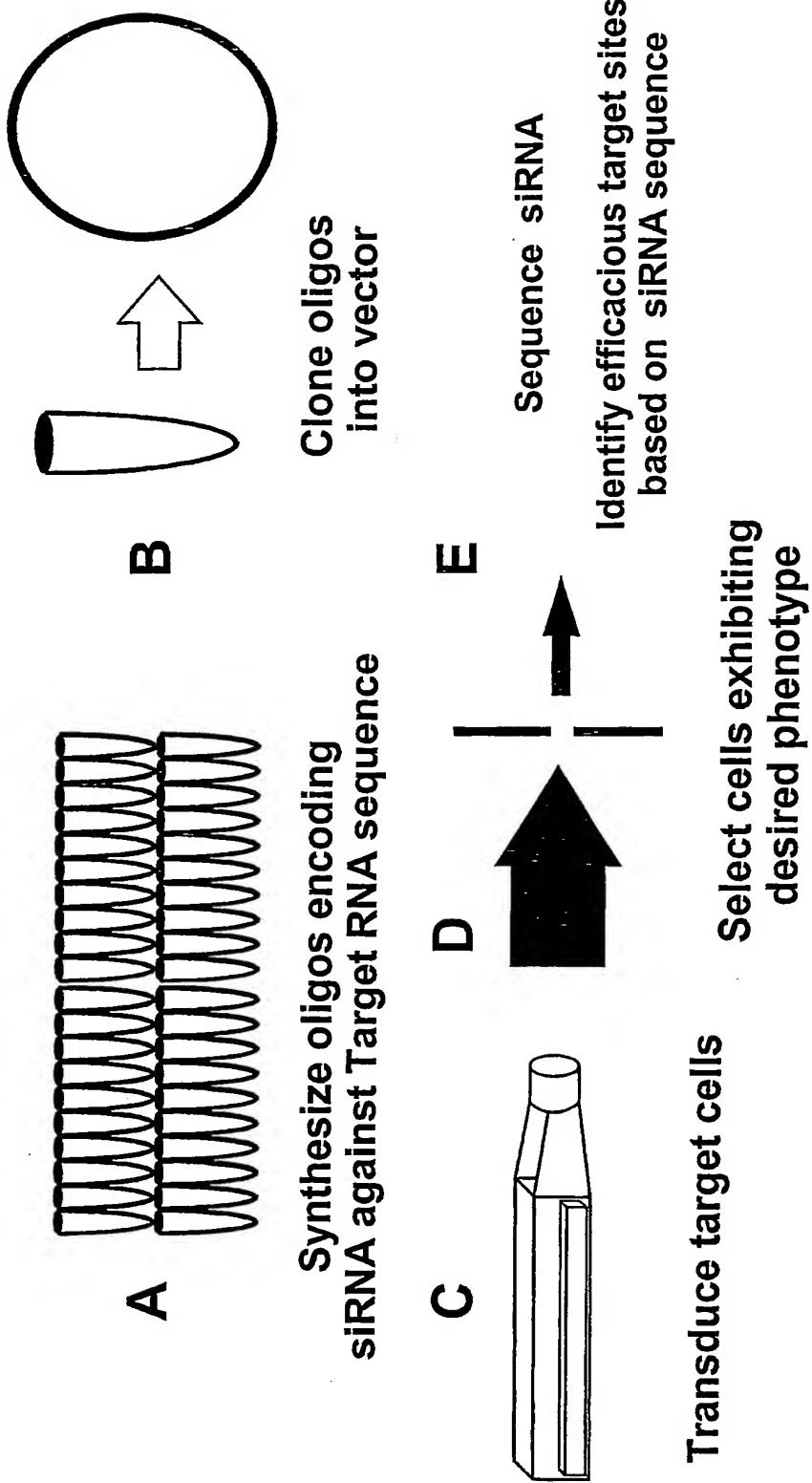
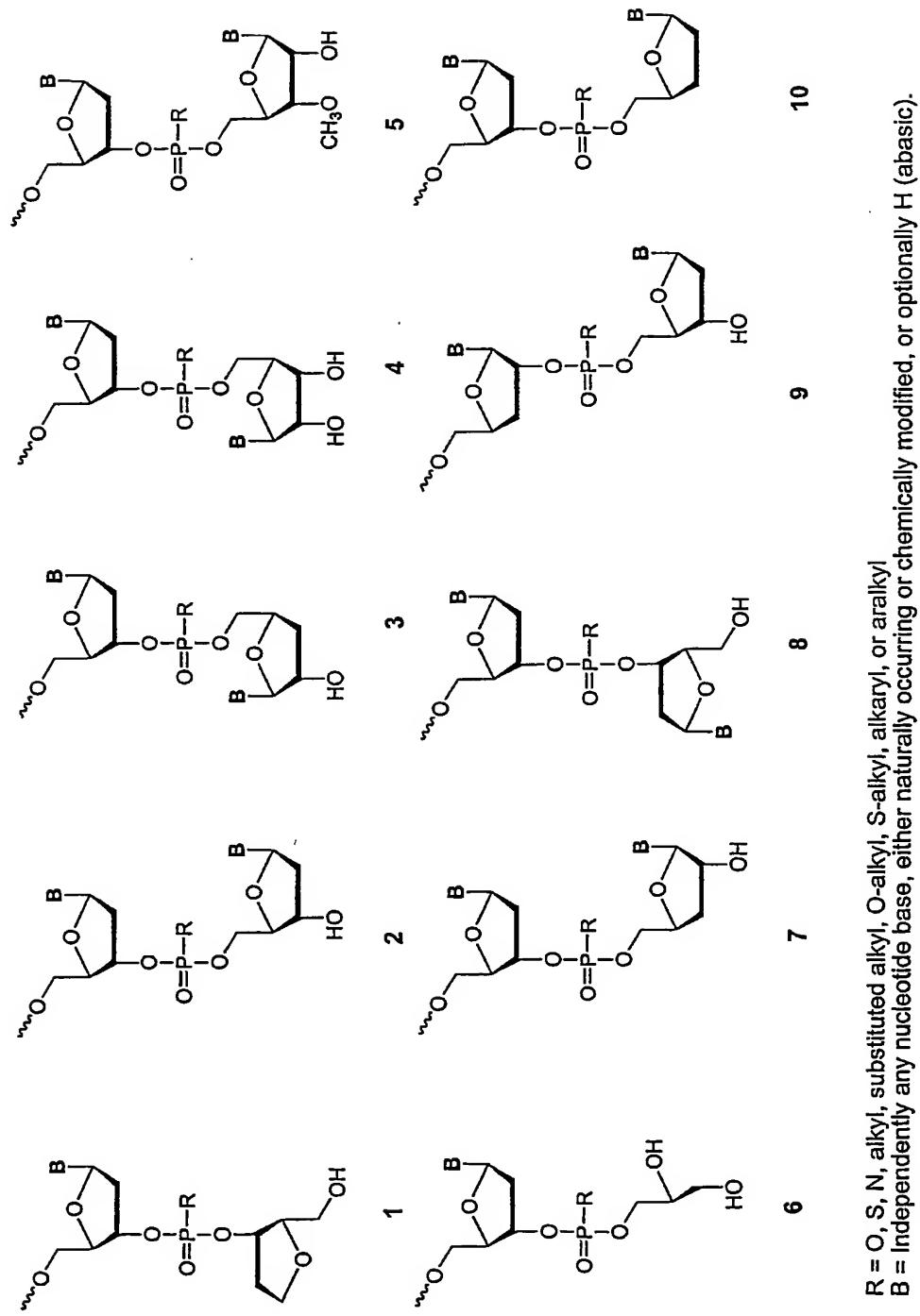


Figure 10

R = O, S, N, alkyl, substituted alkyl, O-alkyl, alkaryl, or aralkyl, or optionally H, or chemically modified, or optionally H (abasic).
B = Independently any nucleotide base, either naturally occurring or chemically modified, or optionally H (abasic).

Figure 11: Modification Strategy

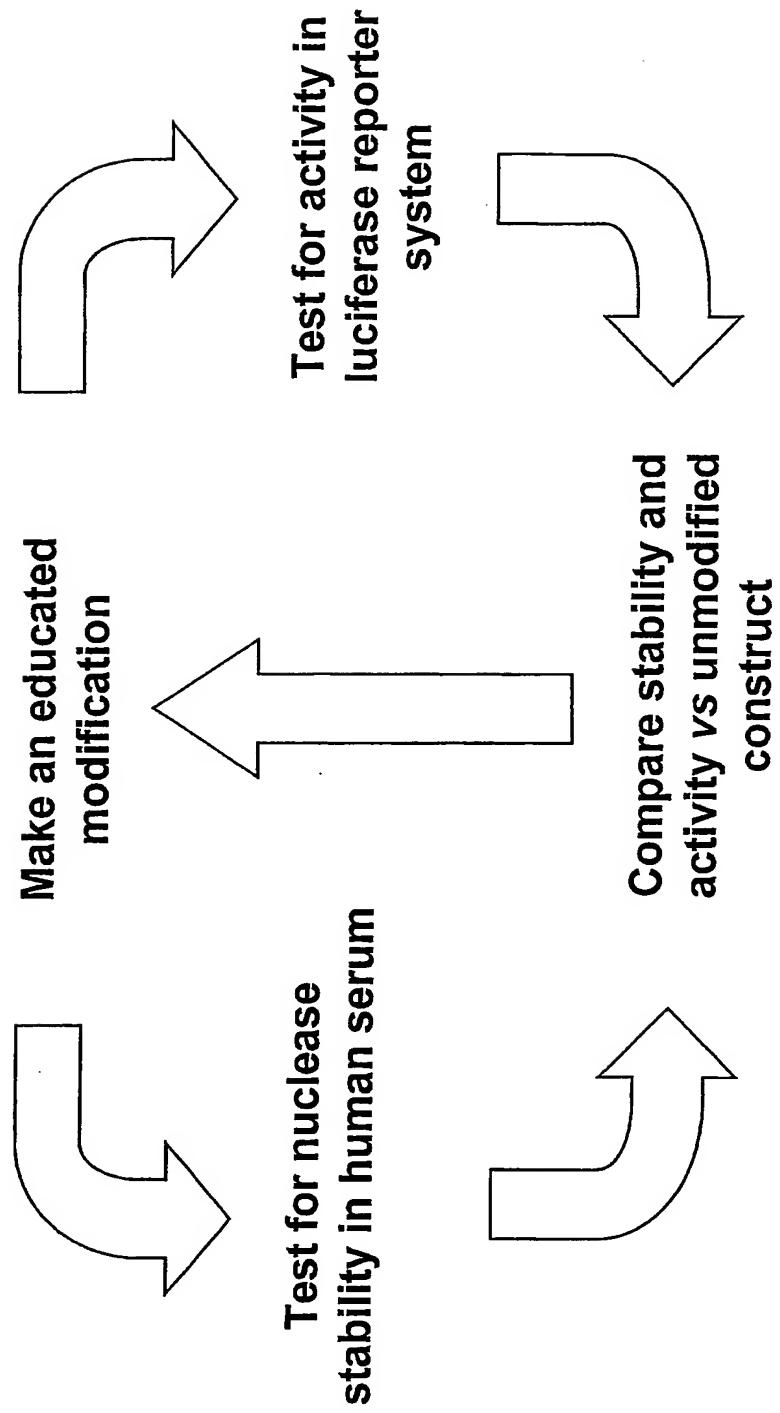


Figure 12: Phosphorylated siNA constructs

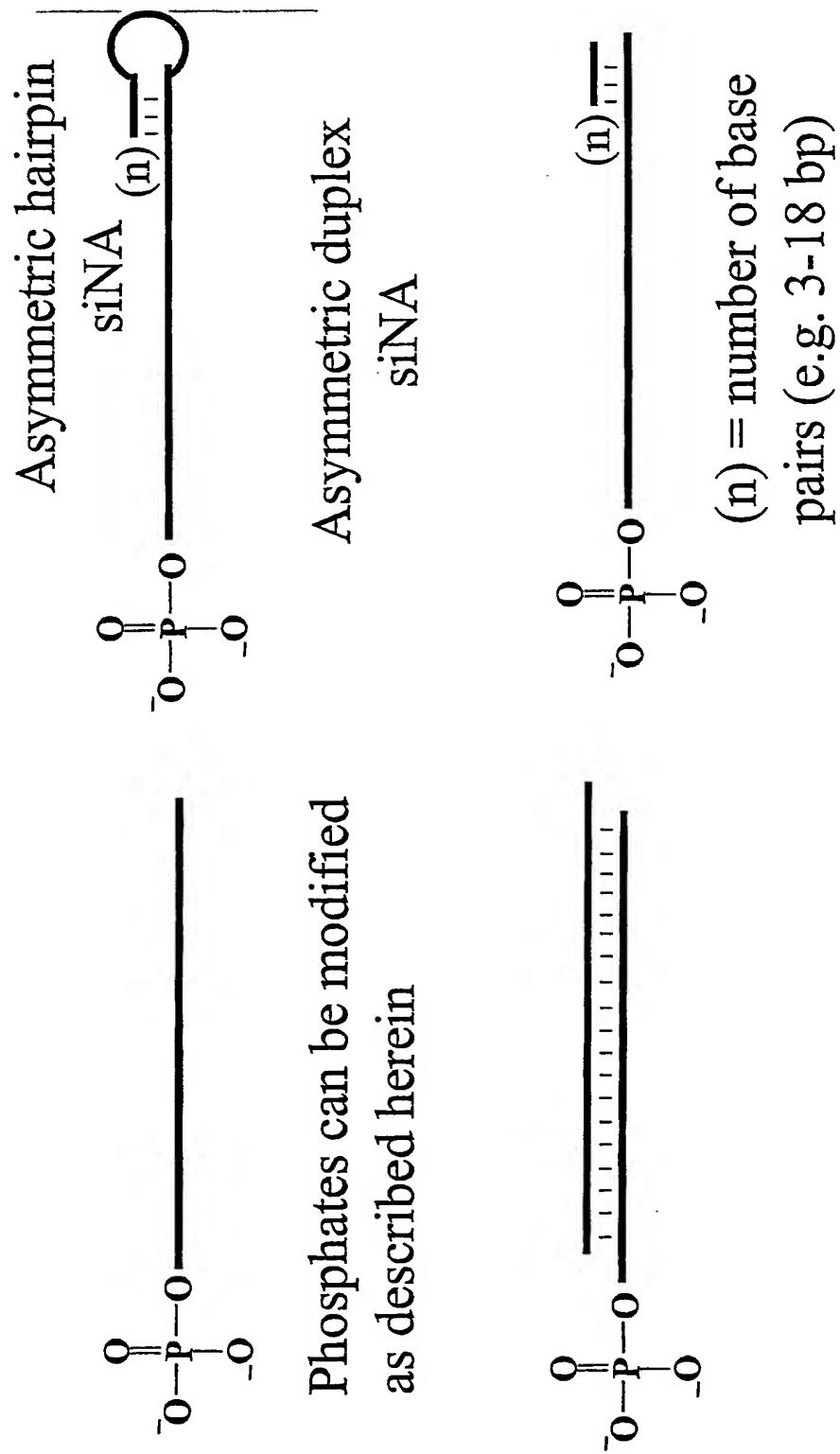


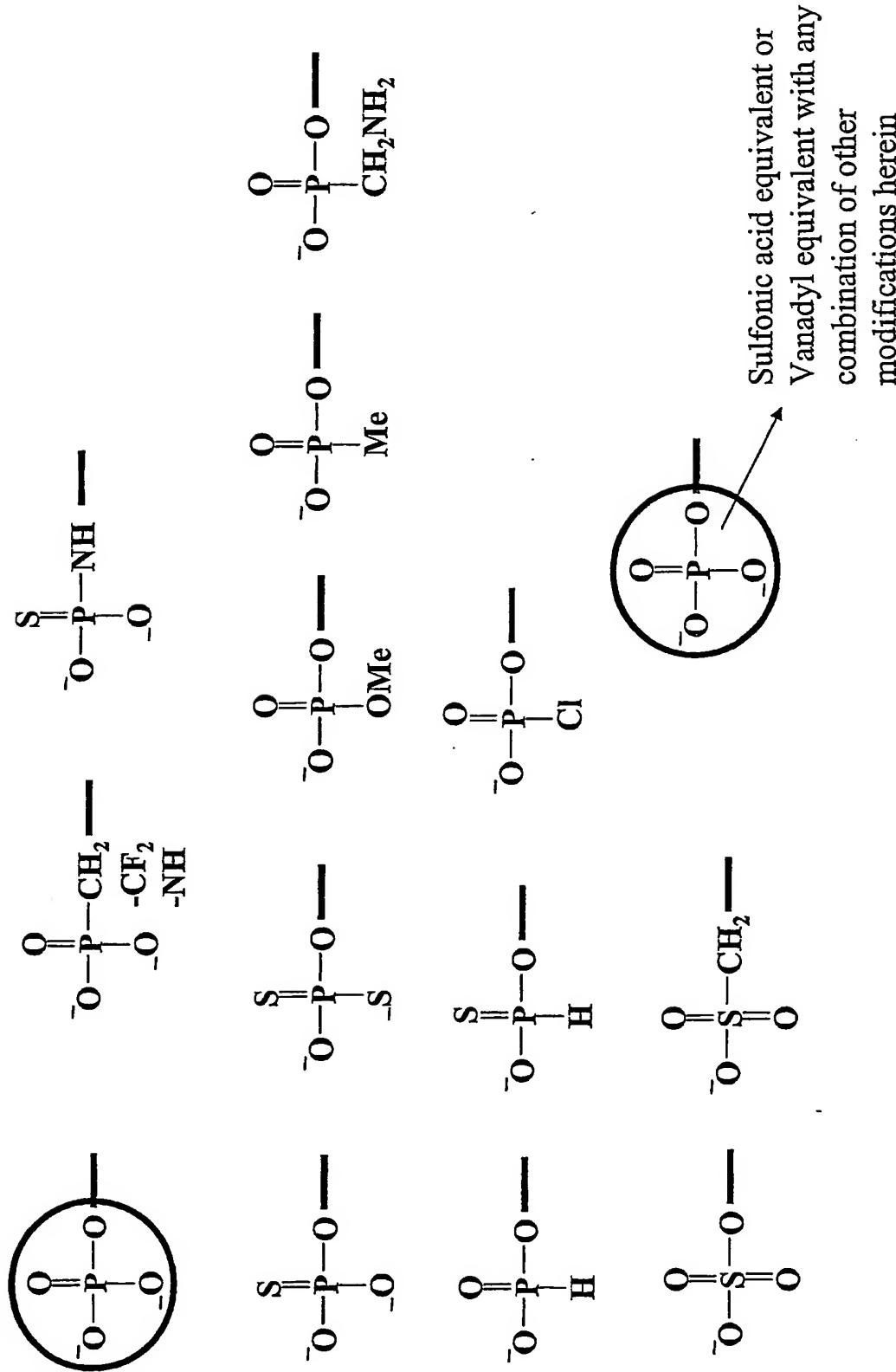
Figure 13: 5'-phosphate modifications

Figure 14A: Duplex forming oligonucleotide constructs that utilize Palindrome or repeat sequences

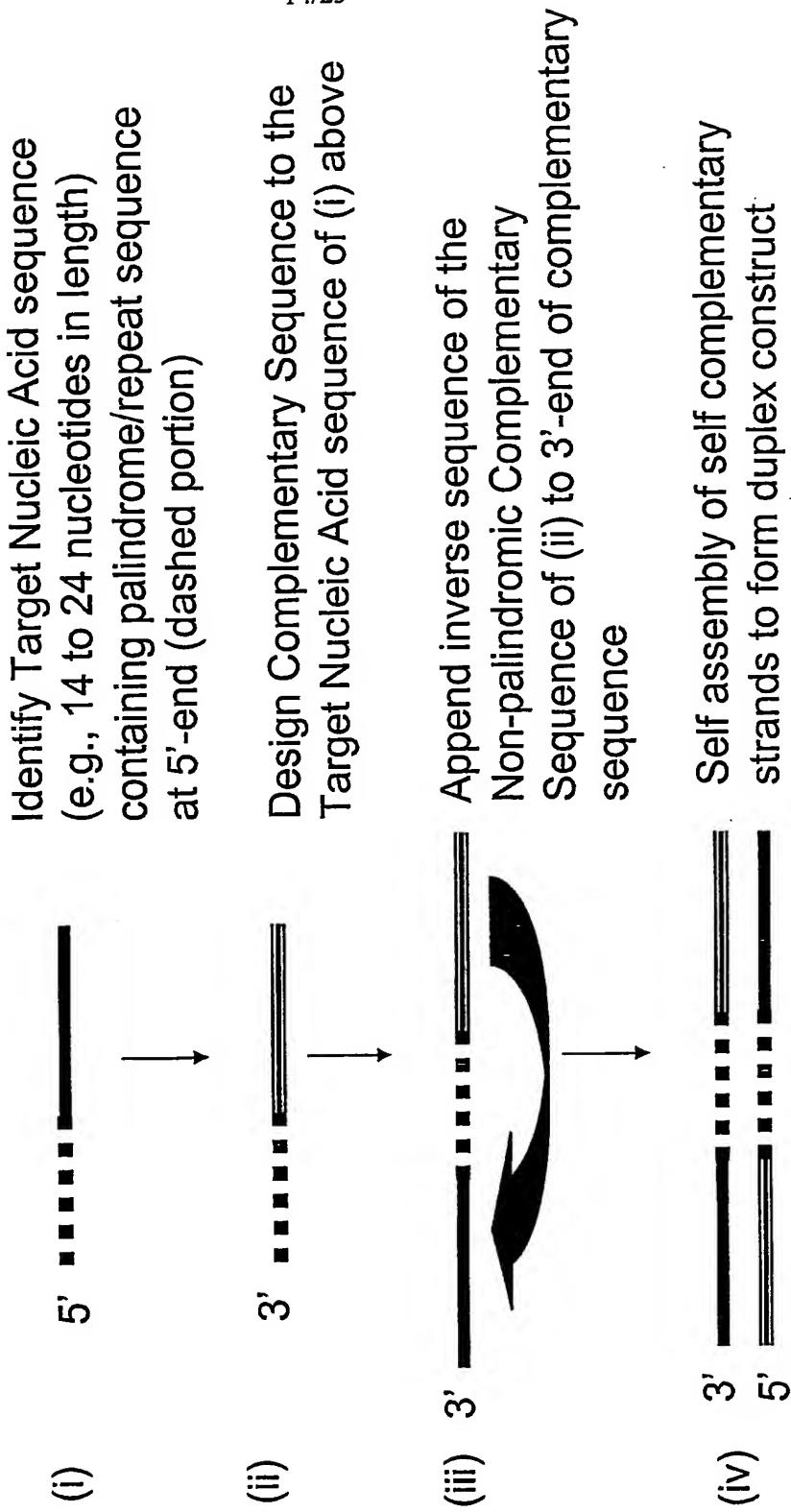


Figure 14B: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence

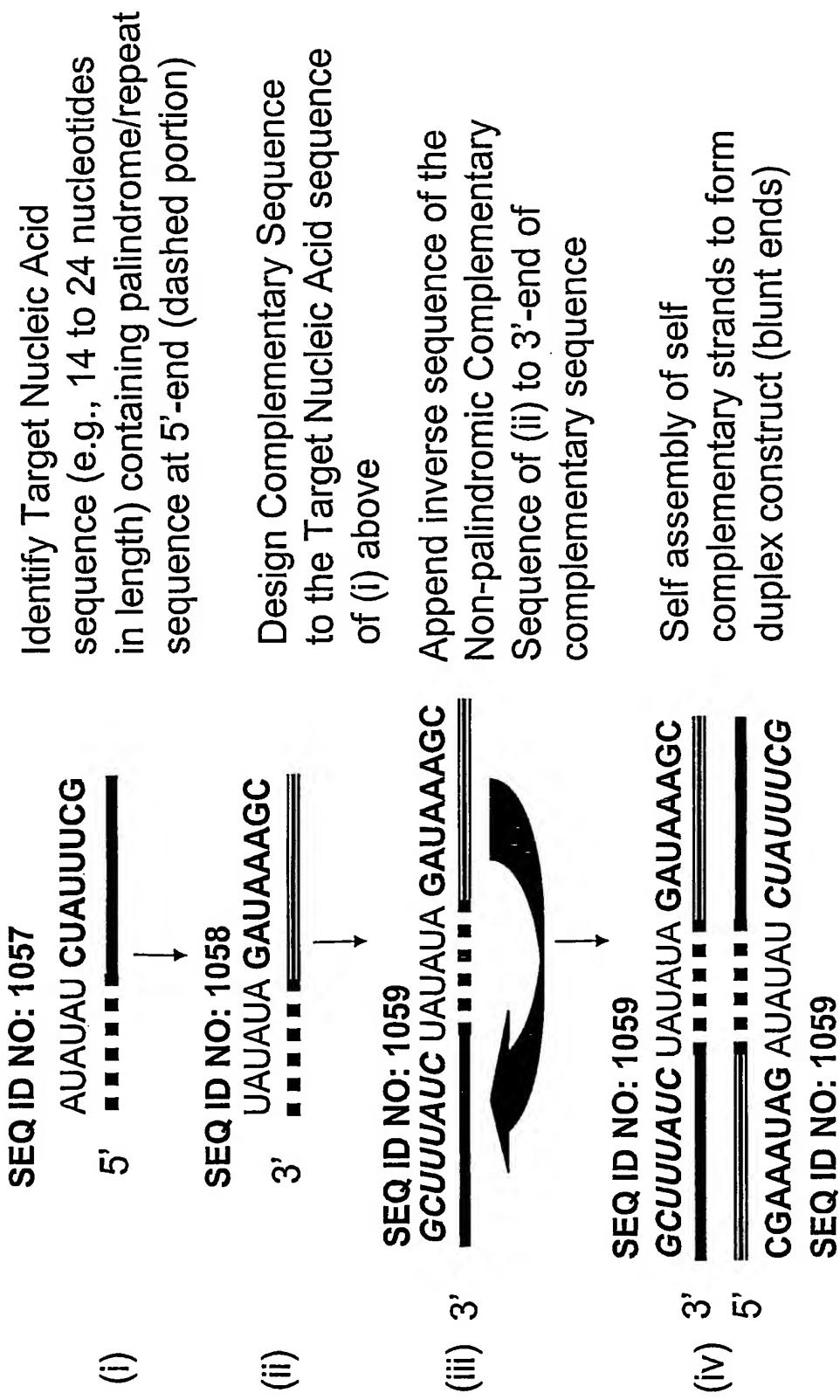


Figure 14C: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly

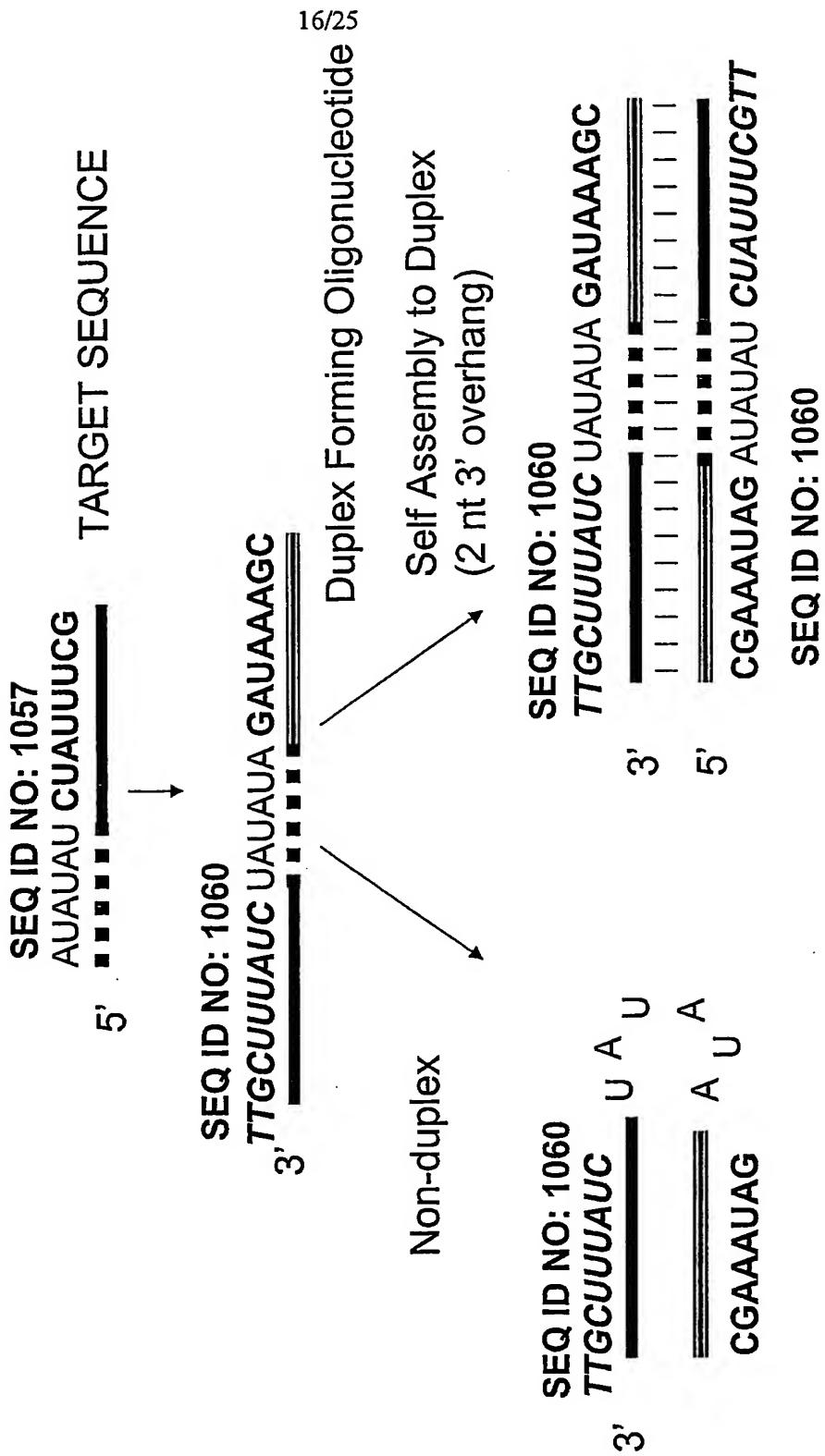


Figure 14D: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly and inhibition of Target Sequence Expression

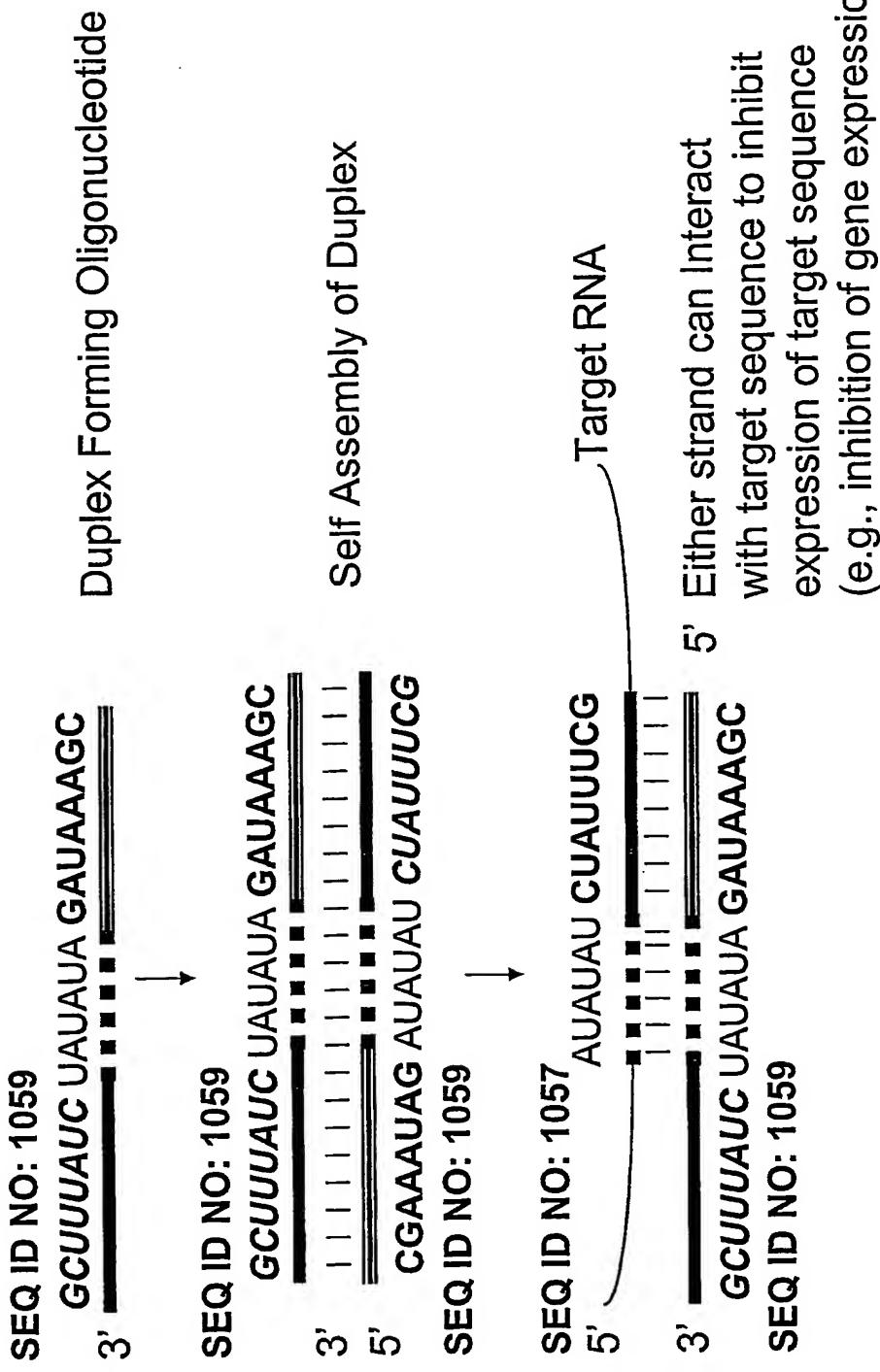


Figure 15: Duplex forming oligonucleotide constructs that utilize artificial palindrome or repeat sequences

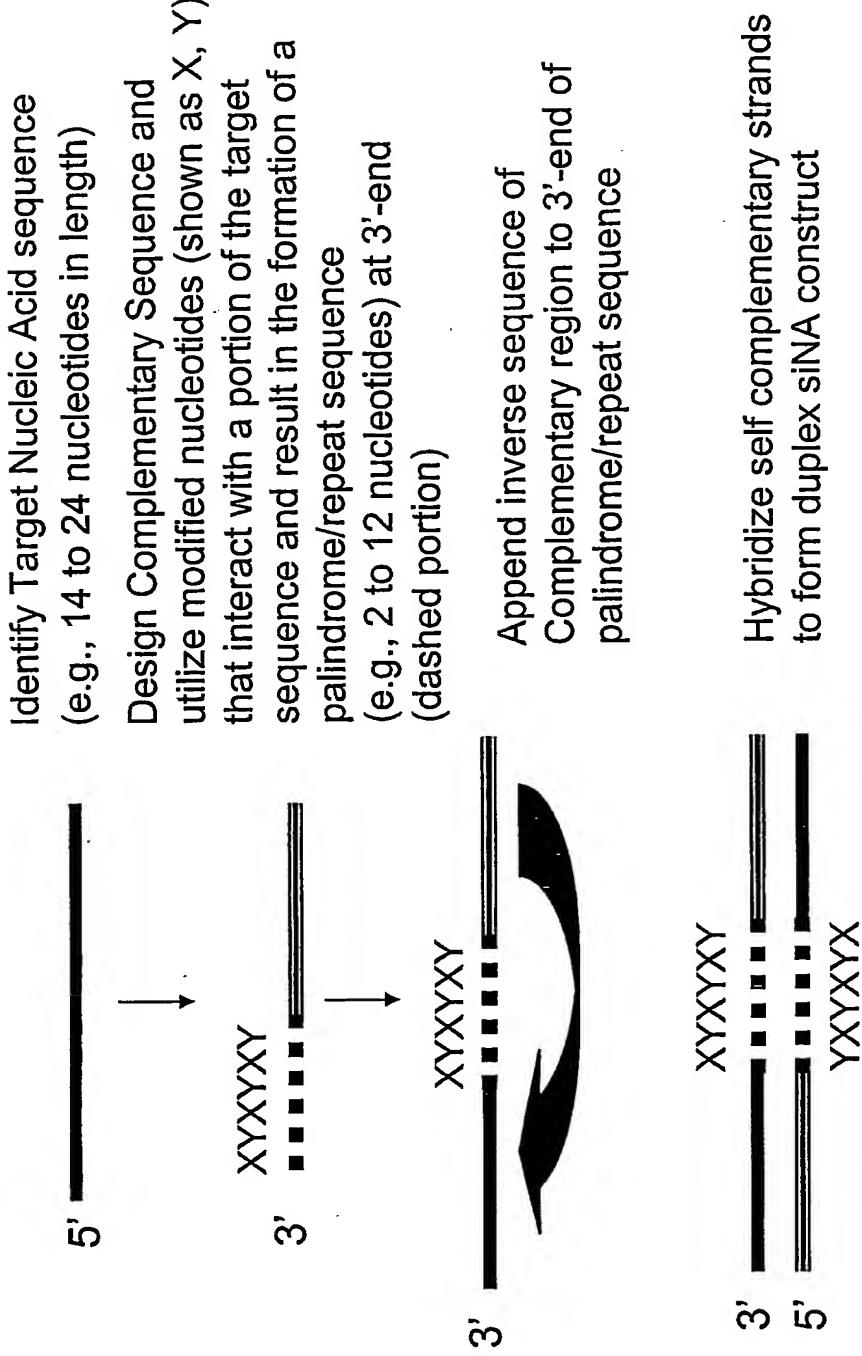


Figure 16: Examples of double stranded multifunctional siRNA constructs with distinct complementary regions

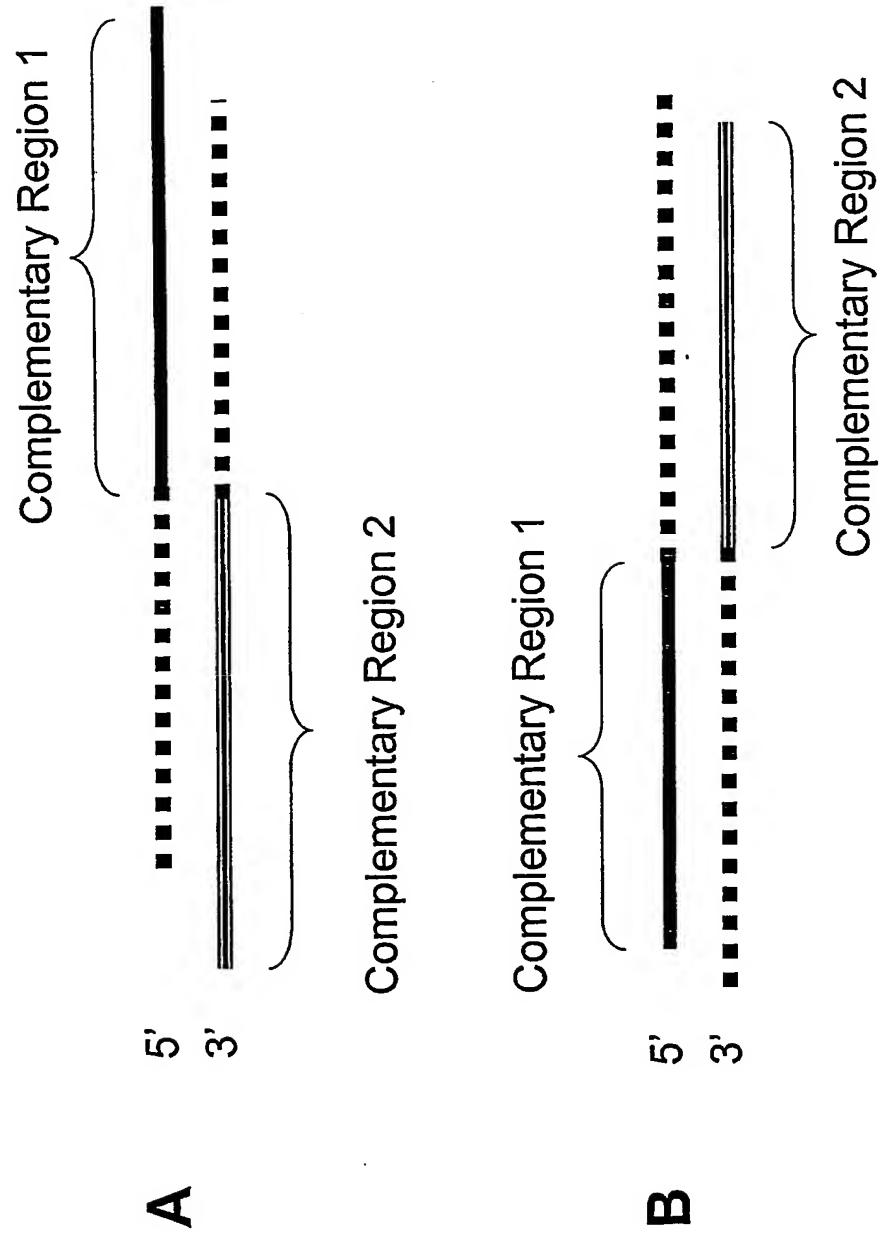


Figure 17: Examples of hairpin multifunctional siRNA constructs with distinct complementary regions

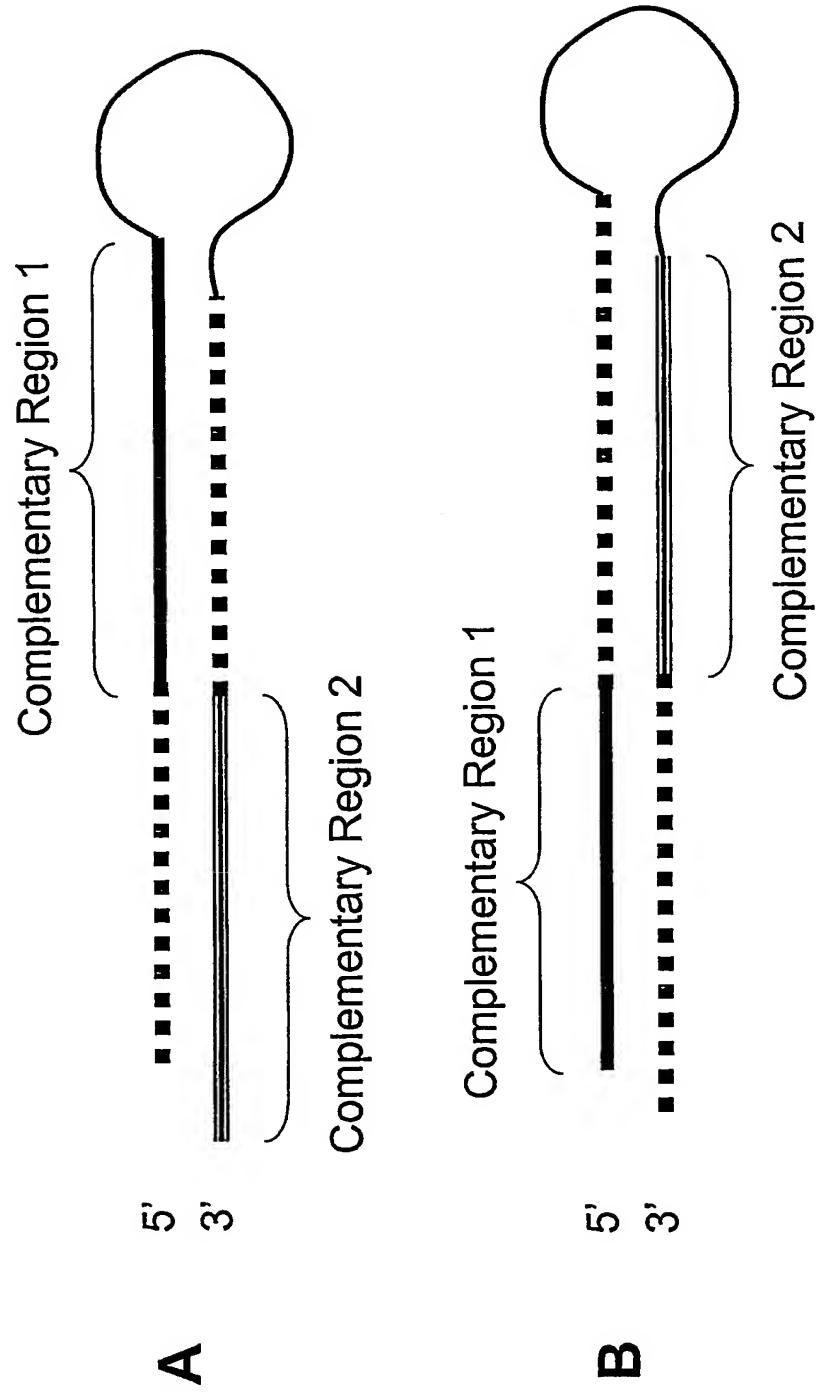
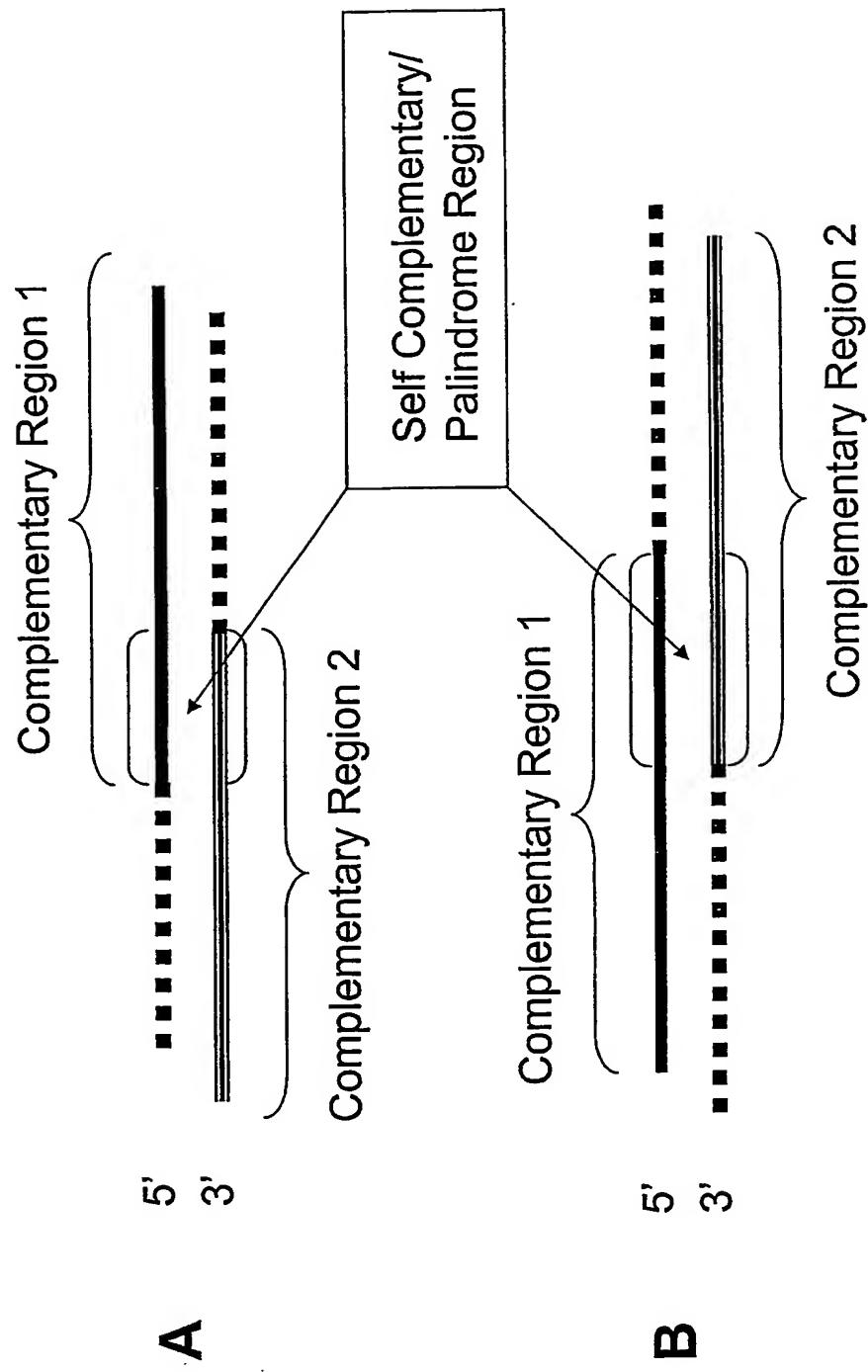


Figure 18: Examples of double stranded multifunctional siRNA constructs with distinct complementary regions and a self complementary/palindrome region



22/25

Figure 19: Examples of hairpin multifunctional sINA constructs with distinct complementary regions and a self complementary/palindrome region

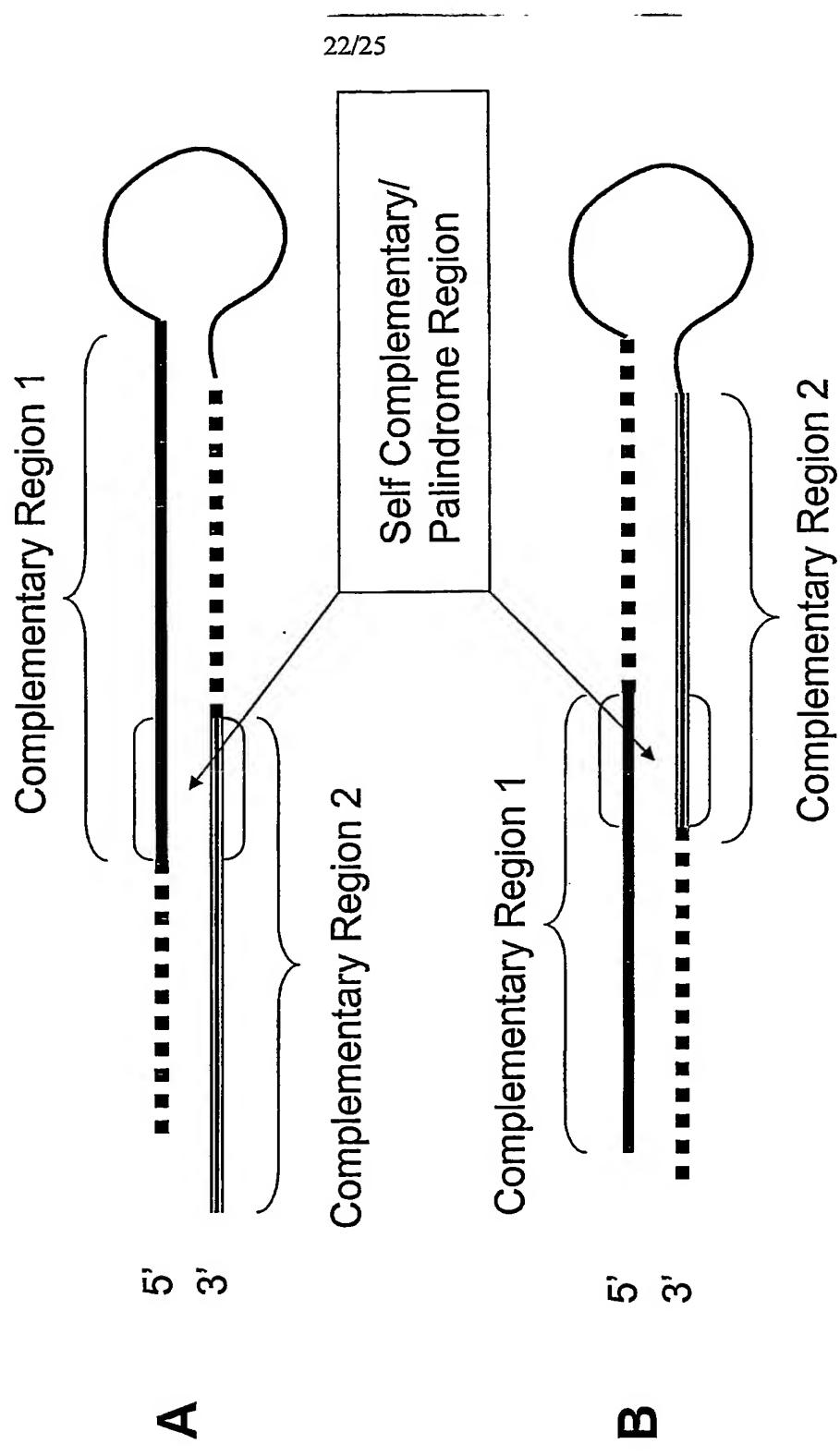


Figure 20: Example of multifunctional siRNA targeting two Separate Target nucleic acid sequences

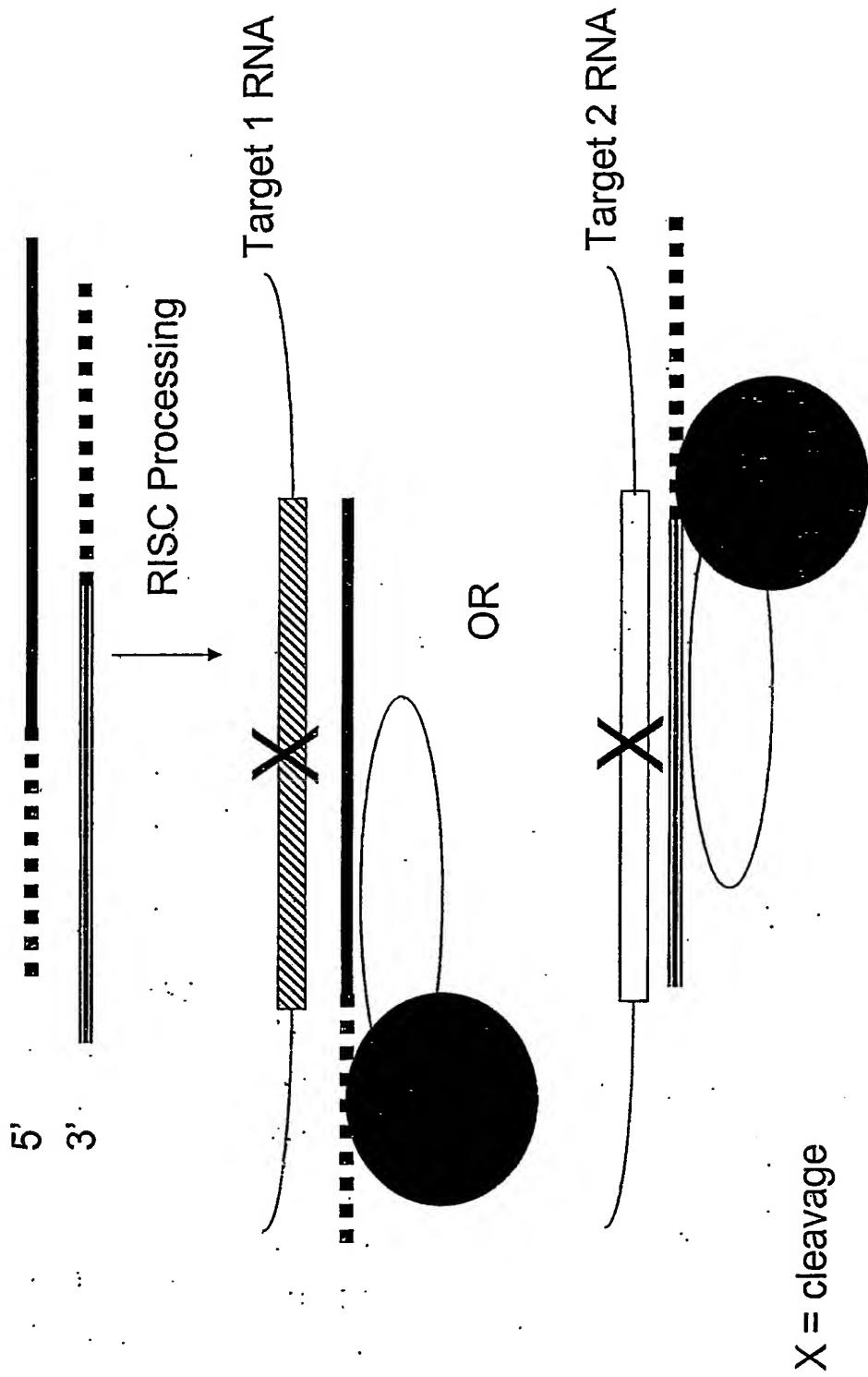


Figure 21: Example of multifunctional siNA targeting two regions within the same target nucleic acid sequence

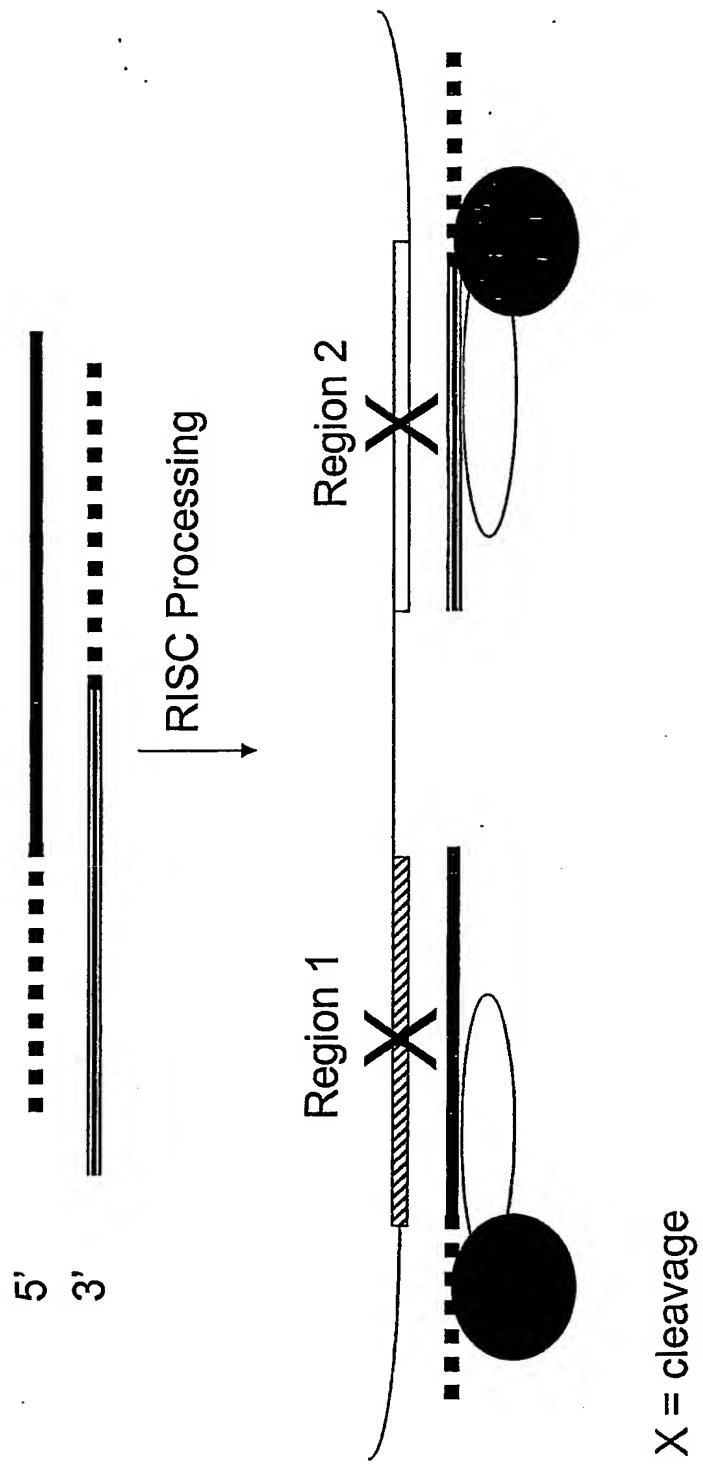


FIGURE 22